Citation:

Tannock LR, O'Brien KD, Knopp RH, Retzlaff B, Fish B, Wener MH, Kahn SE, Chait A. Cholesterol feeding increases C-reactive protein and serum amyloid A levels in lean insulin-sensitive subjects. *Circulation.* 2005 Jun 14; 111(23): 3,058-3,062.

PubMed ID: 15939816

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To study the effects of egg feeding on C-reactive protein (CRP) and serum amyloid A (SAA) in a cohort of health, community-dwelling individuals stratified according to their degree of obesity and insulin resistance.

Inclusion Criteria:

Described elsewhere.

Exclusion Criteria:

Described elsewhere.

Description of Study Protocol:

Recruitment

- Subjects in this study were participants in another study done to examine the effects of insulin resistance and obesity on lipid and lipoprotein responses to egg feeding
- Recruitment for that study is described elsewhere.

Design

- Randomized controlled trial
- The present study evaluated measurements form before and after the four-egg-per-day visits.

Dietary Intake/Dietary Assessment Methodology

Subject completed three-day food records at the beginning and end of each intervention period to

assess compliance with study protocol.

Intervention

- All subjects were counseled to follow the National Cholesterol Education Program (NCEP) Step 1 diet
- Subjects ingested zero, two, or four eggs per day for four-week periods in random order, with each intervention period separated by a four-week washout period
- Maintenance of stable weight was emphasized
- Subjects were given individual frozen daily portions of egg preparation (homogenized natural eggs)
- The four-egg preparation consisted of 68g egg yolk, 20g Egg Beaters egg substitute, and 20g water and provided 253kcal, 13.4g protein, 21g fat, 871mg cholesterol and 6.5g saturated fat.

Statistical Analysis

- Tests for significant differences among the three groups were performed by two-way ANOVA evaluating the effect of group and sex, with pairwise multiple comparisons made with the Holm-Sidak method
- The effects of egg feeding on various parameters were analyzed by paired T-tests when the variables were satisfactory for parametric tests or by Wilcoxon signed-rank tests
- Because CRP and SAA values were not normally distributed, regression analyses with these variables were performed with logarithmically transformed values
- The strength of associations of CRP and SAA with lipoprotein values was evaluated by linear regression on each variable separately, unadjusted for covariates.
- Data were considered significant at (two-sided) $P<0.05$.

Data Collection Summary:

Timing of Measurements

Subjects ingested zero, two or four eggs per day for four-week periods in random order, with each intervention period separated by a four-week washout period. Measurements were taken at the beginning and end of each intervention period.

Dependent Variables

CRP and SAA levels were determined on deeply frozen blood samples.

Independent Variables

Egg consumption.

Control Variables

- Obesity status
- Insulin resistance status.

Description of Actual Data Sample:

- *Attrition (final N):*
    - N=201 subjects who completed the four-egg-per-day intervention

- Subjects were divided into three groups:
  - Lean insulin sensitive (LIS)
  - Lean insulin resistant (LIR)
  - Obese insulin resistant (OIR).
- Obese was considered 27.5kg/m^2 or more, insulin sensitive was 4.2 x 10^{-4} µU per ml or more and insulin resistant was 4.2 x 10^{-4} µU per ml or more.

Subject Characteristics

	LIS	LIR	OIR
N	66	76	59
Sex (male/female, N)	23/43	32/44	27/32
Age, year	49.2±1.2	55.3±1.3	53.7±1.2
Weight, kg	66.9±1.5	71.8±1.2	90.7±1.8
BMI, kg/m2	23.3±0.3	24.5±0.2	31.4±0.5

- *Location:* United States.

Summary of Results:

Egg Feeding and Changes in CRP and SAA

- Egg feeding was associated with a significant increase in levels of both CRP and SAA in the LIS group only (P<0.001). With the LIS group and for all subjects, CRP was highly correlated with the change in SAA (LIS: R=0.955, P<0.001; all Subjects: R=0.754, P<0.001)
- Body weight did not change with egg feeding.

Egg Feeding and Changes in Lipoproteins

- Egg feeding increased non-HDL-C only in the LIS group (P<0.001)
- Egg feeding was associated with significant increases in HDL-C in all three groups (P<0.01).

Lack of Correlation Between Changes in CRP or SAA and Changes in Lipoproteins

- Within the LIS group, the change in non-HDL-C was not correlated with changes in either CRP or SAA
- There were no correlations between changes in CRP or SAA and changes in HDL-C in any group.

Author Conclusion:

- Egg feeding was associated with significant increases in CRP and SAA levels in LIS subjects
- Egg feeding was associated with a significant increase in non-HDL-C in LIS subjects. However, this non-HDL change was not correlated with a change in either CRP or SAA.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	???
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	???
2.2.	Were criteria applied equally to all study groups?	???
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	???
4.1.	Were follow-up methods described and the same for all groups?	???
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	???
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	???
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	???
7.6.	Were other factors accounted for (measured) that could affect outcomes?	No
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	No
8.6.	Was clinical significance as well as statistical significance reported?	Yes

8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes